

Supporting Information

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Table 1S. Levels of POB-DNA adducts in the nasal olfactory mucosa, nasal respiratory mucosa, oral mucosa, and pancreas of NNK-, (R)-NNAL-, and (S)-NNAL-treated rats.

A. Nasal olfactory mucosa

Treatment	Time (weeks)	POB-DNA adducts (fmol/mg DNA)				Total
		<i>O</i> ² -POB-Cyt	7-POB-Gua	<i>O</i> ² -POB-dThd	<i>O</i> ⁶ -POB-dGuo	
NNK	1	ND ^a	63.8 ± 22.7	93.0 ± 21.6	3.6 ± 5.1	160 ± 49
	2	ND	91.5 ± 4.1	141 ± 21	3.6 ± 5.0	236 ± 12
	5	ND	104 ± 16	266 ± 22	3.9 ± 5.5	373 ± 11
	10	3.7 ± 0.7	67.8 ± 12.9	261 ± 26	1.1 ± 1.9	333 ± 37
	16	ND	60.0 ± 7.8	277 ± 28	ND	337 ± 36
	20	ND	63.9 ± 20.3	295 ± 22	ND	359 ± 43
(R)-NNAL	1	ND	4.8 ± 6.8	ND	ND	4.8 ± 6.8
	2	ND	10.2 ± 1.3	26.5 ± 2.3	ND	36.7 ± 1.0
	5	ND	8.8 ± 0.1	31.2 ± 3.8	ND	40.0 ± 3.7
	10	ND	10.1 ± 0.8	42.6 ± 2.1	ND	52.7 ± 1.2
	16	ND	8.4 ± 0.1	39.7 ± 3.6	ND	48.1 ± 3.6
	20	ND	5.4 ± 0.2	33.3 ± 4.0	ND	38.7 ± 3.8
(S)-NNAL	1	ND	75.0 ± 0.9	90.3 ± 4.9	3.1 ± 4.4	168 ± 10
	2	ND	94.0 ± 13.3	137 ± 6	4.3 ± 6.1	236 ± 25
	5	ND	80.8 ± 0.2	231 ± 6	3.0 ± 4.2	315 ± 10
	10	0.8 ± 1.4	61.8 ± 15.4	230 ± 65	2.2 ± 3.8	295 ± 77
	16	ND	49.6 ± 13.0	235 ± 47	ND	285 ± 60
	20	ND	47.8 ± 3.1	235 ± 30	ND	283 ± 33

B. Nasal respiratory mucosa

Treatment	Time (weeks)	POB-DNA adducts (fmol/mg DNA)				Total
		<i>O</i> ² -POB-Cyt	7-POB-Gua	<i>O</i> ² -POB-dThd	<i>O</i> ⁶ -POB-dGuo	
NNK	1	35.9 ± 51.3	322 ± 232	355 ± 216	40.4 ± 35.5	753 ± 503
	2	19.9 ± 34.4	461 ± 236	694 ± 335	59.6 ± 58.9	1235 ± 630
	5	37.4 ± 29.5	561 ± 284	1048 ± 474	48.2 ± 22.4	1695 ± 791
	10	18.6 ± 3.5	518 ± 63	1462 ± 325	49.2 ± 24.7	2048 ± 387
	16	29.2 ± 14.3	495 ± 187	1761 ± 672	61.7 ± 44.5	2316 ± 908
	20	24.7 ± 29.0	433 ± 267	1617 ± 831	36.3 ± 32.5	2111 ± 1129
(R)-NNAL	1	ND	29.1 ± 5.8	35.8 ± 13.1	ND	64.9 ± 18.9
	2	ND	49.9 ± 14.2	75.3 ± 13.1	ND	125 ± 27
	5	ND	55.6 ± 26.5	125 ± 38	ND	180 ± 64
	10	ND	58.0 ± 12.8	185 ± 53	ND	243 ± 66
	16	ND	44.2 ± 23.9	172 ± 52	ND	217 ± 72
	20	ND	42.7 ± 13.5	195 ± 44	ND	238 ± 57
(S)-NNAL	1	5.7 ± 9.9	307 ± 141	370 ± 121	41.4 ± 24.6	724 ± 291
	2	35.1 ± 60.8	493 ± 139	704 ± 132	64.7 ± 20.6	1297 ± 339
	5	ND	633 ± 27	1338 ± 20	94.6 ± 5.5	2066 ± 13
	10	8.6 ± 7.5	403 ± 112	1258 ± 481	51.9 ± 35.8	1722 ± 615
	16	11.0 ± 9.7	396 ± 152	1415 ± 554	38.5 ± 28.5	1860 ± 726
	20	33.4 ± 17.6	377 ± 172	1451 ± 581	41.1 ± 27.7	1902 ± 784

C. Oral mucosa

Treatment	Time (weeks)	POB-DNA adducts (fmol/mg DNA)				
		<i>O</i> ² -POB-Cyt	7-POB-Gua	<i>O</i> ² -POB-dThd	<i>O</i> ⁶ -POB-dGuo	Total
NNK	1	ND	10.5 ± 18.2	59.6 ± 16.9	ND	70.1 ± 30.4
	2	ND	37.6 ± 33.5	101 ± 19	2.3 ± 3.9	141 ± 19
	5	ND	55.6 ± 12.4	177 ± 30	ND	232 ± 18
	10	ND	49.0 ± 19.0	216 ± 15	ND	265 ± 34
	16	ND	42.4 ± 37.2	240 ± 16	ND	282 ± 52
	20	ND	51.3 ± 14.9	326 ± 74	ND	378 ± 69
(R)-NNAL	1	ND	ND	1.7 ± 3.0	12.2 ± 21.1	13.9 ± 19.8
	2	ND	ND	ND	ND	ND
	5	ND	ND	10.3 ± 9.3	ND	10.3 ± 9.3
	10	ND	ND	13.7 ± 9.3	ND	13.7 ± 12.3
	16	ND	ND	7.9 ± 13.7	ND	7.9 ± 13.7
	20	ND	ND	3.8 ± 6.6	ND	3.8 ± 6.6
(S)-NNAL	1	ND	14.3 ± 13.4	31.7 ± 27.5	ND	46.0 ± 40.3
	2	ND	24.5 ± 21.3	78.1 ± 15.8	ND	103 ± 13
	5	ND	22.8 ± 19.8	138 ± 19	ND	160 ± 5
	10	ND	22.8 ± 19.8	185 ± 17	ND	208 ± 16
	16	ND	25.6 ± 22.2	210 ± 21	ND	235 ± 4
	20	ND	27.8 ± 24.1	227 ± 24	ND	255 ± 34

D. Pancreas

Treatment	Time (weeks)	POB-DNA adducts (fmol/mg DNA)				
		<i>O</i> ² -POB-Cyt	7-POB-Gua	<i>O</i> ² -POB-dThd	<i>O</i> ⁶ -POB-dGuo	Total
NNK	1	ND	27.4 ± 0.4	38.4 ± 13.5	ND	65.7 ± 13.9
	2	ND	32.5 ± 4.4	55.1 ± 0.9	ND	87.6 ± 3.6
	5	ND	41.0 ± 1.2	107 ± 13	ND	149 ± 13
	10	ND	41.5 ± 14.1	133 ± 3	ND	174 ± 17
	16	ND	31.7 ± 2.5	150 ± 26	ND	182 ± 28
	20	ND	26.7 ± 6.7	130 ± 15	ND	157 ± 22
(R)-NNAL	1	ND	ND	2.2 ± 1.9	ND	2.2 ± 1.9
	2	ND	ND	5.0 ± 2.0	ND	5.0 ± 2.0
	5	ND	ND	8.0 ± 2.2	ND	8.0 ± 2.2
	10	ND	ND	11.9 ± 1.9	ND	11.9 ± 1.9
	16	ND	ND	11.9 ± 2.9	ND	11.9 ± 2.9
	20	ND	ND	11.4 ± 2.4	ND	11.4 ± 2.4
(S)-NNAL	1	ND	24.2 ± 1.0	30.9 ± 2.6	ND	55.1 ± 2.1
	2	ND	28.7 ± 6.5	51.6 ± 6.7	ND	80.3 ± 12.9
	5	ND	31.2 ± 2.2	95.7 ± 7.3	ND	127 ± 9
	10	ND	40.3 ± 2.0	125 ± 16	ND	165 ± 15
	16	ND	29.6 ± 4.2	131 ± 14	ND	161 ± 18
	20	ND	26.4 ± 1.2	149 ± 26	ND	175 ± 23

a. ND, not detected.

Table 2S. Levels of PHB-DNA adducts in the nasal olfactory mucosa, nasal respiratory mucosa, oral mucosa, and pancreas of NNK-, (R)-NNAL-, and (S)-NNAL-treated rats.

A. Nasal olfactory mucosa

Treatment	Time (weeks)	PHB-DNA adducts (fmol/mg DNA)			
		7-PHB-Gua	<i>O</i> ² -PHB-dThd	<i>O</i> ⁶ -PHB-dGuo	Total
NNK	1	58.5 ± 2.3	115 ± 35	21.1 ± 4.3	195 ± 37
	2	98.7 ± 9.2	164 ± 35	36.5 ± 0.0	299 ± 45
	5	142 ± 8	93.5 ± 29.6	45.8 ± 2.6	281 ± 19
	10	93.6 ± 19.2	75.5 ± 49.1	29.6 ± 7.4	199 ± 23
	16	76.1 ± 7.7	247 ± 310	24.2 ± 6.5	347 ± 325
	20	83.0 ± 26.2	357 ± 312	20.4 ± 2.4	461 ± 283
(R)-NNAL	1	410 ± 71	382 ± 173	55.8 ± 8.7	848 ± 111
	2	543 ± 72	833 ± 97	59.5 ± 6.3	1435 ± 163
	5	691 ± 148	331 ± 190	43.6 ± 1.7	1065 ± 163
	10	676 ± 62	629 ± 254	46.6 ± 3.0	1352 ± 319
	16	490 ± 35	1682 ± 968	32.1 ± 3.6	2204 ± 1007
	20	439 ± 81	1373 ± 880	23.0 ± 4.0	1835 ± 803
(S)-NNAL	1	43.4 ± 1.5	117 ± 1	18.4 ± 1.3	179 ± 4
	2	73.9 ± 0.7	142 ± 22	24.2 ± 6.0	240 ± 29
	5	84.8 ± 19.6	121 ± 126	27.1 ± 2.1	233 ± 109
	10	70.0 ± 10.7	75.4 ± 0.2	22.8 ± 5.6	168 ± 16
	16	63.1 ± 11.4	226 ± 234	18.3 ± 2.0	308 ± 220
	20	47.5 ± 2.5	260 ± 248	13.0 ± 0.3	321 ± 245

B. Nasal respiratory mucosa

Treatment	Time (weeks)	PHB-DNA adducts (fmol/mg DNA)			
		7-PHB-Gua	<i>O</i> ² -PHB-dThd	<i>O</i> ⁶ -PHB-dGuo	Total
NNK	1	323 ± 19	507 ± 78	161 ± 32	991 ± 27
	2	569 ± 55	907 ± 190	247 ± 65	1724 ± 310
	5	687 ± 145	235 ± 175	226 ± 11	1148 ± 308
	10	435 ± 19	190 ± 62	220 ± 6	845 ± 36
	16	600 ± 76	1526 ± 1815	340 ± 100	2466 ± 1991
	20	517 ± 109	1715 ± 1155	285 ± 1	2518 ± 1047
(R)-NNAL	1	1523 ± 27	1793 ± 587	330 ± 92	3646 ± 706
	2	2346 ± 675	4154 ± 214	457 ± 76	6957 ± 537
	5	3567 ± 1000	1955 ± 55	400 ± 12	5921 ± 1067
	10	3525 ± 192	3565 ± 993	401 ± 27	7491 ± 773
	16	3563 ± 945	10110 ± 2100	338 ± 83	14010 ± 1070
	20	3300 ± 446	9014 ± 7497	306 ± 18	12620 ± 7033
(S)-NNAL	1	295 ± 22	475 ± 33	147 ± 7	917 ± 62
	2	366 ± 79	750 ± 127	201 ± 33	1318 ± 172
	5	455 ± 8	582 ± 638	317 ± 9	1354 ± 655
	10	495 ± 96	244 ± 176	269 ± 5	1007 ± 267
	16	382 ± 104	1275 ± 1331	246 ± 61	1903 ± 1495
	20	454 ± 85	1401 ± 913	272 ± 9	2127 ± 837

C. Oral mucosa

Treatment	Time (weeks)	PHB-DNA adducts (fmol/mg DNA)			
		7-PHB-Gua	<i>O</i> ² -PHB-dThd	<i>O</i> ⁶ -PHB-dGuo	Total
NNK	1	ND ^a	ND	ND	ND
	2	ND	ND	ND	ND
	5	ND	33.9 ± 23.1	ND	33.9 ± 23.1
	10	ND	15.7 ± 12.1	ND	15.7 ± 12.1
	16	ND	99.9 ± 127.9	ND	99.9 ± 127.9
	20	ND	139 ± 197	ND	139 ± 197
(R)-NNAL	1	ND	ND	ND	ND
	2	ND	133 ± 188	10.7 ± 15.2	144 ± 203
	5	205 ± 28	72.2 ± 44.8	19.6 ± 5.1	297 ± 12
	10	110 ± 156	188 ± 266	31.1 ± 0.9	330 ± 421
	16	187 ± 13	834 ± 267	ND	1020 ± 280
	20	189 ± 49	844 ± 585	ND	1033 ± 536
(S)-NNAL	1	ND	ND	ND	ND
	2	ND	ND	ND	ND
	5	ND	ND	ND	ND
	10	ND	14.7 ± 2.1	ND	14.7 ± 2.1
	16	ND	86.1 ± 111.6	ND	86.1 ± 111.6
	20	ND	ND	ND	ND

D. Pancreas

Treatment	Time (weeks)	PHB-DNA adducts (fmol/mg DNA)			
		7-PHB-Gua	<i>O</i> ² -PHB-dThd	<i>O</i> ⁶ -PHB-dGuo	Total
NNK	1	ND	ND	ND	ND
	2	ND	25.0 ± 1.4	ND	25.0 ± 1.4
	5	11.9 ± 10.4	41.9 ± 10.8	ND	53.8 ± 16.5
	10	ND	107 ± 34	ND	107 ± 34
	16	19.2 ± 5.5	109 ± 5	ND	128 ± 9
	20	13.6 ± 12.0	113 ± 10	ND	126 ± 15
(R)-NNAL	1	47.6 ± 16.2	67.7 ± 8.4	4.6 ± 0.7	120 ± 25
	2	70.0 ± 0.6	110 ± 16	4.2 ± 0.6	184 ± 16
	5	91.2 ± 11.8	249 ± 48	6.2 ± 2.0	346 ± 54
	10	97.5 ± 14.2	373 ± 56	3.6 ± 3.1	474 ± 60
	16	94.0 ± 10.4	445 ± 35	4.9 ± 1.0	544 ± 34
	20	73.0 ± 17.7	475 ± 73	4.1 ± 1.1	552 ± 82
(S)-NNAL	1	ND	6.0 ± 10.4	ND	6.0 ± 10.4
	2	ND	36.4 ± 5.6	ND	36.4 ± 5.6
	5	5.0 ± 8.7	50.4 ± 11.3	ND	55.5 ± 19.9
	10	ND	59.1 ± 13.0	ND	59.1 ± 13.0
	16	9.6 ± 8.6	87.9 ± 24.1	ND	97.5 ± 32.3
	20	ND	90.9 ± 4.6	ND	90.9 ± 4.6

a. ND, not detected.